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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,279	07/08/2003	Richard Harkins	51791AUSD1	4679

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,279	HARKINS ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-29,31-41 and 44-46* is/are pending in the application.

4a) Of the above claim(s) *24-29,31-34,36-41 and 44-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 6, 2006 has been entered.

Applicant's amendments and reply received June 6, 2006 are acknowledged.

Claims 1-23, 30, 42, and 43 have been canceled.

Claim 35 has been amended.

Claims 24-29, 31-41 and 44-46 are pending in the instant case.

Claims 24-29, 31-34, 36-41 and 44-46 stand withdrawn from consideration as being drawn to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03, for reasons of record set forth in the Office Action mailed July 5, 2005.

Claim 35 is under examination in the instant office action as it recites a method of destroying a cell that expresses SEQ ID NO:2 by administering an antibody that binds an epitope of SEQ ID NO:2 wherein the epitope is the elected species of SEQ ID NO:10. Note that SEQ ID NO:10 is the same sequence as amino acids 77-91 of SEQ ID NO:2. In light of the prior art, the species election has been withdrawn.

Applicant's amendments to the first line of the specification to update priority information are acknowledged.

Claim Rejections - 35 USC § 102

2. The rejection of claim 35 under 35 U.S.C. 102(b) as being anticipated by Sheppard (WO 98/45442, of record) as evidenced by Kreitman (Exp. Op.

Pharmacother, 2000, 1:1117-1129, of record) has been withdrawn in light of applicant's amendment to the claim received April 6, 2006.

Specifically, Sheppard does not teach that the antibodies used in his method bind the specific epitopes of SEQ ID NO:2 recited in the instant claim. Therefore the rejection has been obviated.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claim 35 stands provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/624,884 due to anticipation of the instant invention for the reasons of record set forth in the office action mailed July 5, 2005.

Applicant has acknowledged the provisional rejection and as indicated that duplicative subject matter will be canceled once claims are otherwise indicated as allowable in the instant application. Since no cancellation has been made, the rejection of record is maintained.

5. Claim 35 stands provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending

Application No. 10/895,183 due to anticipation of the instant invention for the reasons of record set forth in the office action mailed July 5, 2005.

Applicant has acknowledged the provisional rejection and as indicated that duplicative subject matter will be canceled once claims are otherwise indicated as allowable in the instant application. Since no cancellation has been made, the rejection of record is maintained.

The following are new grounds of rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 35 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of destroying a cell expressing the polypeptide of SEQ ID NO:2 by contacting said cell with an immunoconjugate wherein the immunoconjugate comprises a cytotoxic agent and an antibody that binds an epitope selected from the group consisting of amino acids 28-46 of SEQ ID NO:2, 77-91 of SEQ ID NO:2, 188-210 of SEQ ID NO:2, and 263-274 of SEQ ID NO:2, does not reasonably provide enablement for a method of destroying a cell by contacting said cell with immunoconjugates that comprise therapeutic agents or with immunoconjugates that comprise antibodies that bind epitopes 70% identical to the epitopes listed above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has claimed a method of destroying cells that express the polypeptide of SEQ ID NO:2 by contacting said cells with an immunoconjugate comprising an antibody and a therapeutic agent. The specification discloses that cytotoxic agents can

be used therapeutically and provides numerous examples of cytotoxic agents (see particularly lines 8-13 of page 5 and lines 25-29 of page 30 of the instant specification). The specification also discloses additional labels and detectable markers that can be coupled to antibodies for use in diagnostic methods (see particularly lines 15-21 of page 30 and from line 29 of page 30 to line 5 of page 31). The specification does not define the term "therapeutic agent", but the Merriam-Webster OnLine dictionary defines therapeutic as "of or relating to the treatment of disease or disorders by remedial agents or methods <a *therapeutic* rather than a diagnostic specialty>". As such, detectable labels disclosed for use in diagnostic assays are not therapeutic agents. Further, detectable labels such as fluorescent, chemiluminescent and bioluminescent compounds would not be capable killing or destroying a cell. It is noted that the specification teaches that unconjugated antibodies can kill cells via complement mediated cytolysis (see particularly lines 6-17 of page 31) but the claim recites antibody fragments that specifically bind the recited epitopes of SEQ ID NO:2. Antibody fragments are taught as being Fab fragments (see particularly lines 25-30 of page 28). Such antibody fragments lack the constant domain found in whole antibody and therefore they are not recognized by complement and cannot engage in complement-mediated cell lysis (Kipriyanov et al., see entire document). As such the portion of the immunoconjugate that mediates cell killing must be the therapeutic agent and not the antibody. Therefore, only therapeutic agents that comprise cytotoxic activity can be part of the immunoconjugates administered in the claimed method, and the only disclosed therapeutic agents having cytotoxic activity are cytotoxic agents.

The instant claim also recites the epitopes that are bound by the antibody portion of the aforementioned immunoconjugates. The recited epitopes include those that are 70% identical to epitopes selected from the group consisting of amino acids 28-46 of SEQ ID NO:2, amino acids 77-91 of SEQ ID NO:2, amino acids 188-210 of SEQ ID NO:2, and amino acids 263-274 of SEQ ID NO:2. An immunoconjugate of the instant invention must be able to bind the polypeptide of SEQ ID NO:2 if it is to mediate the destruction of a cell expressing the polypeptide of SEQ ID NO:2. Colman teaches that even single amino acids changes within an antigen can effectively abolish antibody

binding to said antigen (Research in Immunology, 1994, 145:33-36, see entire document, particularly the third sentence of the right column of page 33). As such, an immunoconjugate that binds an epitope 70% identical to one of the recited epitopes of SEQ ID NO:2 does not necessarily maintain the ability to bind the polypeptide of SEQ ID NO:2. The specification does not teach which amino acid residues within the disclosed epitopes of SEQ ID NO:2 are required for antibody binding and thus must be maintained or conversely which epitope residues are not essential for antibody binding and thus can be mutated at will. Without additional guidance or direction, a skilled artisan would need to conduct additional undue research to identify immunoconjugates that bind epitopes 70% identical to the disclosed epitopes and retain the ability to bind the polypeptide of SEQ ID NO:2 such that they can be used in the instant claimed method.

Therefore, given that therapeutic agents as disclosed by applicant are not required to be cytotoxic, that agents which are not cytotoxic cannot destroy a cell, that antibody fragments such as Fab lack domains needed for complement-mediated lysis and thus also cannot destroy a cell, and that immunoconjugates comprising antibodies that bind sequences 70% identical to a recited epitope of SEQ ID NO:2 do not necessarily retain the ability to bind the polypeptide of SEQ ID NO:2, a skilled artisan would need to conduct an undue amount of additional research in order to practice the full scope of applicant's claimed method.

8. Claim 35 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed a method of killing cells by administering an immunoconjugate that comprises a therapeutic agent. The specification does not define the term "therapeutic agent" or identify the structural or functional properties required of members of the genus of therapeutic agents. It is noted that the specification discloses

that preferred therapeutic agents are cytotoxic and provides examples of cytotoxic agents (see particularly lines 8-13 of page 5 and lines 25-29 of page 30), and as such cytotoxic agents are clearly a subgenus of therapeutic agents.

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Fri., January 5, 2001, see especially page 1106 column 3).

As discussed above, the specification does not disclose a structure common to all therapeutic agents and does not define the functional properties required of therapeutic agents. Further, the subgenus of cytotoxic agents does not support the broader genus of therapeutic agents because the common functional activity of the subgenus, i.e. cytotoxicity, is not a functional activity present in all members of the genus of therapeutic agents. In light of this, one of skill in the art would reasonably conclude that the disclosure fails to provide adequate written description of the genus of "therapeutic agents" and therefore applicant was not in possession of the genus of "therapeutic agents" at the time the invention was filed.

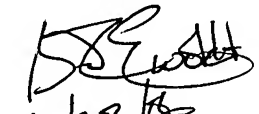
9. No claim is allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
June 14, 2006



G.R. EWOLDT, PH.D.
PRIMARY EXAMINER